REMARKS

Applicants thank the Examiner for rejoining the inventions of groups 1-4, claims 1-9, and examining the claims together.

With entry of the instant amendment claims 21-43 have been cancelled and claim 44 has been entered. Claims 10-20 were withdrawn by the Examiner as drawn to non-elected inventions. Claims 1-9 and 44 are therefore currently under examination. Applicants cancellation of claims 21-43 is without prejudice to subsequent revival for prosecution.

The amendments to the claims add no new matter.

Claim 1 has been amended to cancel subject matter related to non-elected inventions. The cancellation of the subject matter is made without prejudice to subsequent revival for prosecution.

Claim 1 has also been amended to recite an amino acid sequence comprising at least 95% identity to the amino acid sequence of SEQ ID NO:2. Support can be found, *e.g.*, on page 9, lines 4-10.

Claim 44 recites that the nucleic acid comprises the sequence set forth in SEQ ID NO:1. Support can be found, *e.g.*, in Example 1, pages 56-58; and on page 2, lines 14-16 and page 7, lines 7-13.

The objections/rejections will be addressed in the order presented in the February 28, 2005 Office Action.

Specification

The first paragraph on page 1 has been amended to update the status of the parent provisional application and requested by the Examiner.

Rejection under 35 U.S.C. § 112, first paragraph--enablement

Claims 1-9 are rejected as allegedly lacking enablement. The Examiner contends that although applicant have shown that amplification and overexpression of a PRC17 polynucleotide in example 1, there is no nexus between that polynucleotide and a polynucleotide

encoding SEQ ID NO:2. In particular, the Examiner alleges that one of skill cannot extrapolate the teachings of the specification to the enablement of the claims because it is not possible to determine the identity of the PRC17 polynucleotide that is overexpressed and/or amplified, and accordingly can't determine whether it encodes SEQ ID NO:2. To the extent that the rejection applies to the amended claims, Applicants respectfully traverse.

As the Examiner knows, the test of enablement is whether one of skill in the art can make and use the invention without undue experimentation (*see, e.g.,* MPEP § 2164.01). In the instant application, Applicants have provided general guidance in how to detect PRC17 nucleic acid and polypeptide sequences (*see, e.g.,* page 26, line 32 through page 29, line 20). Further, Applicants have taught how to use detection of such sequences for the diagnosis of (*see, e.g.*, page 44, lines 5-20). Moreover, Applicants have exemplified detection of PRC17 polynucleotide sequences that undergo increased copy number and increased expression in cancer relative to normal (*see, e.g.,* examples 1 and 2). Applicants have used PCR techniques to show that PRC17 is amplified and overexpressed in cancer. Further, Applicants shave shown that an antibody to a carboxyl terminal sequence of PRC17 detects overexpression of the protein. Moreover, Applicants have shown that PRC17 confers growth advantage in low serum. SEQ ID NO:1 is clearly identified in the specification as PRC17. It encodes SEQ ID NO:2.

The Examiner appears to believe that Applicants may not in fact be detecting a PRC17 gene that encodes SEQ ID NO:2 and is thus ultimately questioning operability of the claimed invention. However, no evidence is provided to support that one of skill would not believe that the polynucleotides that are detected in Applicants' examples encode SEQ ID NO:2. When the examiner concludes that an application is describing an invention that is non-useful, inoperative, or contradicts known scientific principles, the burden is on the examiner to provide a reasonable basis to support this conclusion (*see, e.g.,* MPEP 2164.07(I.)(B)). Here, the Examiner has failed to meet this burden.

As additional evidence that Applicants have detected that amplification and overexpression of a nucleic acid encoding SEQ ID NO:2, Applicants provide herewith in Exhibit 1 a publication by Pei *et al.*, (*Cancer Res.* 62:5420-5424, 2003). Pei *et al.* additionally

describe that the amplified gene at 17q12, which was identified by Applicants, encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:2. PRC17 was identified at the epicenter of a novel 17q12 amplicon that is amplified in cancer. A full-length PRC17 cDNA was obtained (*see, e.g.*, page 5421, column 2, and Fig. 1 on page 5422, which indicates that PRC17 cDNA sequence was deposited under accession AF540953, a copy of which is attached to Pei *et al.*). This cDNA encodes SEQ ID NO:2. Pei *et al.* further confirm that *PRC17* mRNA and protein is overexpressed in cancer (*see, e.g.*, page 5421, second column, second full paragraph). Last, we note that the journal *Cancer Research* is a peer-reviewed journal. Thus, the publication of this paper provides evidence that those of skill in the art believe that *PRC17* is amplified and/or overexpressed in cancer and that there is a nexus between the *PRC17* gene and SEQ ID NO:2.

With regard to the Examiner's enablement rejections relating to detection of nucleic acids encoding polypeptides that have at least 85% identity to SEQ ID NO:2, although Applicants disagree, in order to expedite prosecution, claim 1 has been amended to recite a polypeptide comprising at least 95% identity to SEQ ID NO:2. Such sequences include polymorphic variants. Applicants have taught how to determine whether *PRC17* is amplified and/or overexpressed in cancer (*see, e.g.*, example 1, pages 56-58 and the general guidance in the specification (*e.g.*, pages 26-29). The rejection provides no evidence or reasoning that one of skill could not reasonably expect such techniques to also be applicable to polymorphic variants of SEQ ID NO:2. Thus, in view of the disclosure in the specification, the amount of experimentation in practicing the claimed invention is not undue. Accordingly, Applicants have met the enablement requirement.

In view of the foregoing, Applicants respectfully request withdrawal of the rejection.

Rejection under 35 U.S.C. § 112, first paragraph--written description

Claims 1-9 were rejected as allegedly lacking adequate written descriptive support in the specification. The Examiner alleges that Applicants have not described nucleic acids

encoding polypeptides that have at least 85% identity to SEQ ID NO:2. Although, Applicants disagree, in order to expedite prosecution, claim 1 has been amended to recite a polypeptide having at least 95% identity to SEQ ID NO:2.

As the Examiner knows, written description does not required that the disclosure as originally filed provide *in haec verba* support for claimed subject matter (*see, e.g., Purdue Pharma L.P. V. Faulding, Inc.* 230 F.3d 1320, 1323, 56 USPQ2d 1481, 1483 (Fed. Cir. 2000)). It is not necessary that the application describe the claim limitations exactly, but only to the extent that one of ordinary skill in the art would recognize from the disclosure that appellants invented the subject matter (*In re Herschler*, 591 F.2d 693, 200 USPQ 711 (CCPA 1979).

The Federal Circuit has expressly considered the application of the written description requirement to inventions in the field of biotechnology. See, *University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The Court held that the written description requirement can be fulfilled in any number of ways, so long as the specification describes the invention in sufficient detail that one skilled in the art can clearly conclude that the inventor invented the claimed invention. For a chemical invention, an adequate description "requires a precise definition, such as by structure, formula, chemical name, or physical properties...." (119 F.3d at 1568, 43 USPQ2d at1406.) The Court also addressed the manner by which a genus of cDNAs might be described, when it stated:

> A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. (also 119 F.3d at 1568, 43 USPQ2d at 1406). (emphasis added)

Applicants have provided such a structural feature, the reference sequence(s). Claim 1 recites 95% identity to the reference sequence, which relates to highly conserved variants or polymorphic alleles. In view of the structural hallmark set forth in the claims and the overall high degree of identity to the reference sequence, Applicants have complied with the written description requirement.

Furthermore, the Examiner alleges that Applicants have not provided the complete structure of any polynucleotide encoding SEQ ID NO:2 that will function as claimed. To the extent that the rejection applies to the amended claims, Applicants respectfully traverse. The claims as filed and as amended recite structural hallmarks, sequences that amplify and/or hybridize to the sequence to be detected and a reference polypeptide sequence. The MPEP unequivocally states that "in the molecular biology arts, if an applicant discloses an amino acid sequence, it would be unnecessary to provide an explicit disclosure of nucleic acid sequences that encoded the amino acid sequence. Since the genetic code is widely known, a disclosure of an amino acid sequence would provide sufficient information such that one would accept that an applicant was in possession of the full genus of nucleic acid encoding a given amino acid sequence" (MPEP §2163 (II)(3)(a)(ii)). Thus, the genus of allelic variants that encode SEQ ID NO:2 are acknowledged in the MPEP to be readily described by those in the art when the polypeptide reference sequence is provided. Applicants have thus satisfied the written description requirement. Withdrawal of the rejection is therefore requested.

Rejection under 35 U.S.C. § 112, second paragraph)

Claims 4 and 5 were rejected as allegedly indefinite for lacking proper antecedent basis. Applicants believe that the amendment to claim 4 addresses this rejection and therefore respectfully request its withdrawal.

Rejection under 35 U.S.C. § 102(b)

Claims 1-5, and 9 were rejected as allegedly anticipated by Onno *et al.* (DNA and Cell Biol. 12:107-118, 1993). The Examiner alleges that Onno *et al.* teach a method of detecting Ewing sarcoma cancer cells by detecting a nucleic acid encoding a PRC17 polypeptide and that this reference therefore anticipates the instant invention. To the extent that the rejection applies to the amended claims, Applicants respectfully traverse.

The Examiner states that for examination purposes, the Examiner is assuming that the claims is drawn to detecting a nucleic acid that encodes at least 2 consecutive amino acids of

SEQ ID NO:2 and that the nucleic acid detected is not limited to a sequence encoding SEQ ID NO:2. Applicants believe that the amendments to the claims overcome this rejection.

The Examiner also states that TRE17 wt has 100% identity to SEQ ID NO:2, referring to Appendix I of the Office Action, which provides an alignment. Applicants acknowledge that the polypeptide alignment shows 100% identity; however, it is not clear from the Appendix precisely when the comparison sequence was disclosed in the art. SEQ ID NO:2 (or a nucleic acid encoding SEQ ID NO:2) is not present in Onno *et al.* Moreover, Onno *et al.* does not teach or suggest that amplification and/overexpression of a nucleic acid encoding SEQ ID NO:2 (or a sequence having 95% identity to SEQ ID NO:2) is associated with cancer. If the Examiner believes that SEQ ID NO:2 is somehow disclosed in Onno *et al.*, or another prior art reference, Applicants respectfully request that the Examiner explicitly indicate where the sequence is disclosed. In view of the foregoing, Applicants respectfully request withdrawal of the rejection.

Rejection under 35 U.S.C. § 103, obviousness

Claims 1 and 6-8 were rejected as allegedly obvious over Onno *et al.* in view of Pollack *et al.* The Examiner contends that Onno *et al.* disclose a polypeptide that comprises at least 85% amino acid identity to an amino acid sequence of SEQ ID NO:2 that was detected in human Ewing sarcoma cells. The Examiner concludes that it would therefore have been obvious that the currently claimed sequences would be amplified and/or overexpressed in cancer cells. To the extent that the rejection applies to the amended claims, Applicants respectfully traverse.

As the Examiner knows, in order to establish a *prima facie* case of obviousness, the rejection must demonstrate that: (1) there is some suggestion or motivation to modify the reference or combine the reference teachings; (2) there is a reasonable expectation of success: and (3) the prior art references suggest all the claim elements. *See, e.g.*, MPEP § 2143; *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991). Further, the teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. (*see, In re Vaeck, supra*). The argument advanced by the

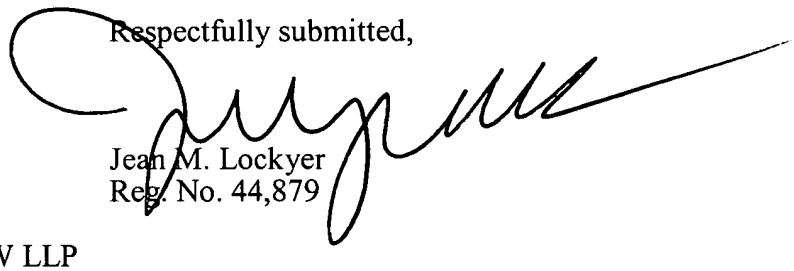
Examiner fails. As noted above, Onno *et al.* does not disclose a nucleic acid encoding SEQ ID NO:2 (or a polypeptide having at least 95% identity to SEQ ID NO:2), nor does the reference disclose that *PRC17* is amplified and/or overexpressed in any kind of cancer. Thus, the cited references fail to teach or suggest all of the claim elements. Applicants therefore respectfully request withdrawal of the rejection.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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